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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,935	05/04/2005	Rubina Mian	GRT/3772-38	9653

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EXAMINER	
WOOD, AMANDA P	
ART UNIT	PAPER NUMBER
1657	
MAIL DATE	DELIVERY MODE
04/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,935	MIAN ET AL.	
	Examiner	Art Unit	
	AMANDA P. WOOD	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-14,16,17,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-14,16,17,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 December 2007 has been entered.

Claims 1-2, 5-14, 16-17, and 23-24 have been examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 10 December 2007 has been considered by the examiner and a signed and initialed copy is attached to this Office Action.

Claim Objections

Claim 1 is objected to because of the following informalities: In lines 1-2 of claim 1, Applicant recites "an individual, which is a mammal or bird". An "individual" is normally considered to relate to humans, not to generic non-human mammals, or to birds. Appropriate correction is required.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 5-14, 16-17, and 23-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In particular, Applicant recites that phrase "changed physiological status" in claim 1, line 2. Applicant does not provide a definition for this phrase in the instant specification which would allow one of skill in the art to practice the claimed invention. In lines 6-7 of page 3 of the instant specification, Applicant explains that "coping capacity is an *in vitro* assessment of the individual's current physiological status" and further explains in lines 3-4 that "the ability of neutrophils to respond to such *in vitro* challenge after a stressful event is defined as the individual's coping capacity." Therefore, Applicant has not reasonably described what would encompass a "changed physiological status" of an individual other than to point out that coping capacity is one means of assessing a current physiological status, has not complied with the written description requirement.

Furthermore, Claim 1 recites the phrase "psychological stressor" in lines 3, 11, and 18. Based upon the lack of a clear definition for a "psychological stressor," it is unclear what Applicant intends to encompass such a "psychological stressor" other than the few exemplary stressors given in the examples of the application, and therefore, Applicant has failed to comply with the written description requirement.

Claim 1 further recites the term "basal" in line 7. Applicant does not provide any definition or guidance in the instant specification for what this term should mean. In particular, Applicant repeatedly refers to "basal activity," "basal response" and "basal superoxide production" in the specification (see, for example, page 6, line 8, page 9, lines 19-20, and page 17, line 28), but provides no actual definition or particular method of obtaining the basal measurement. It is entirely unclear from the specification whether a basal measurement is made prior to or after test subjects are exposed to the stressor because it appears to differ between the type of subjects being tested (i.e., whether the subject is a non-human animal or a human). In the non-human mammal examples, it appears that all blood samples in test subjects were taken from the subjects after handling, so it is unclear how a basal measurement could have been made in these subjects if a basal measurement should be made prior to exposure to the stressor. In the human examples, it appears that all blood samples in test subjects were taken prior to exposure to the stressor. Based upon the lack of a clear definition in the specification for "basal," and the apparent ambiguity amongst the examples in the instant specification with respect to basal measurements, Applicant has failed to comply with the written description requirement.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, first paragraph for the reasons set forth above.

Claims 1-2, 5-14, 16-17, and 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for determining coping capacity of neutrophils, does not reasonably provide enablement for determining a changed physiological status arising from any psychological stressor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' "(Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the relative skill of those in the art, (6) the amount or

direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

N.B. MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

1-2 .Breadth of the claims and the nature of the invention..

In regard to the method of the invention and the breadth of the claims the broadest interpretation that applies is a method of determining whether any individual, being a mammal or bird, is experiencing changed physiological status arising from exposure to any psychological stressor.

3-4. The state of prior art and the level of predictability in the art.

Ellard et al (Intl J. Psychophys 2001, as cited in IDS 7/2005) specifically teach that short-term (i.e., 15 minutes) psychological stressors are sufficient to activate neutrophils (i.e., release of superoxide anions), and that once activated, neutrophils are unable to respond to opportunistic infections (i.e., unable to produce another superoxide burst), such as invading bacteria, and would thus render the body more susceptible to

disease and possible tissue damage from released enzymes and metabolites (see Ellard et al, pg. 99, col. 2). Furthermore, Kang et al (Brain, Behavior, and Immun. 1996, as cited by Examiner 8/2006) teach that psychological stressors, such as examinations, in a population of students tend to increase superoxide production to levels above baseline levels measured prior to the stressor (i.e., examination period), and further maintain or enhance superoxide levels after the exam period. Therefore, based upon the teachings provided by Kang et al, it would appear that neutrophils in students exposed to psychological stressors such as examinations have the ability to continuously produce superoxide without the reduction in activity discussed by Ellard et al. Based upon this apparent unpredictability in the effect of psychological stressors on subjects (i.e., what would be considered to be a stressor for one test subject may not be a stressor for another, and what may be a control situation for one subject may actually be a stressful situation for another), it appears that the prior art is not in agreement as to what would constitute a psychological stressor, or how neutrophils react to such stressors.

5. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

6-7. The amount of guidance present and the existence of working examples.

Applicant has not provided any definitions for "changed physiological status" or "psychological stressor" in the instant specification. There are no working examples in the instant specification which involve testing any mammal or bird for "changed

physiological status." Since Applicant has not provided any guidance as to what "changed physiological status" is meant to encompass, this phrase is not enabled. The working examples are drawn to measurements of leukocyte coping capacity in non-human mammals, but no guidance is provided with respect to birds or to farmed animals.

The working examples provided for humans do not actually describe coping capacity, but describe "leukocyte responsiveness" and that "an altered responsiveness to PMA indicates *in vivo* changes to the state of leukocyte activation" (see pg. 25, lines 12-13, and pg. 26, line 28, of instant specification). The only working examples Applicant provides for non-human mammals are for wild mammals, for which the psychological stressors are trapping and transport of the mammals, and handling of the mammals. Applicant further provides examples of exposing rats to an unfamiliar environment and exposing mice to social stress (see page 12, lines 11-16 of instant specification). It is unclear from the specification what other types of psychological stressors might be useful in the claimed method.

8. The quantity of experimentation necessary.

The amount of experimentation that is required is undue: while testing for superoxide production in neutrophils before and after exposure to a stressor is routine, a method of determining whether an individual is experiencing changed physiological status from exposure to a psychological stressor is not routine and requires more experimentation. Furthermore, based upon the lack of a nexus between the preamble and the instant method steps (e.g., the steps comprise determining superoxide

production in blood as an indicator of coping capacity, but the preamble comprises determining changed physiological status after exposure to a psychological stressor), it would require undue experimentation to practice the claims as drafted. Therefore, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, first paragraph for the reasons set forth above.

Claims 1-2, 5-14, 16-17, and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the same regime" in line 10. There is insufficient antecedent basis for this limitation in the claim.

Claims 1-2, 5-14, 16-17, and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Claim 1 lacks active steps for providing basal measurements of superoxide production in a test whole blood sample and in a control whole blood sample. Applicant claims limitations

for determining superoxide production "above basal" but does not actually provide any steps for determining the basal superoxide level. Furthermore, in the remarks filed 10 December 2007 Applicant admits that "there must be a basal measurement (prior to stimulation).

Claims 1, 5-14, 16-17, and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Claim 1 lacks an active step for exposing an individual to a psychological stressor. Based upon the preamble of Claim 1, the method requires exposure to a psychological stressor, but the claim lacks any actual method steps drawn to such a limitation.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Maintained Rejections

Claim Rejections - 35 USC § 103

Claims 1-5, 9-11, and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikawa et al (Can J Anaesth 1993) in view of Pfefferkorn (US 5,492,816).

A method is claimed for determining whether an individual is experiencing changed physiological status arising from exposure to a psychological stressor.

Mikawa et al beneficially teach a method wherein

Mikawa et al beneficially teach a method wherein a basal level of superoxide production, or control level, is measured in whole blood samples before anesthesia administration prior to a surgical procedure in infants and neonates. Mikawa et al beneficially teach methods wherein PMA and FMLP are used as inducers for production of superoxide in neutrophils. Mikawa et al further beneficially teach that after surgery, neonates had the greatest suppression of superoxide production by neutrophils, but infants also showed immunosuppression after surgery. Mikawa et al did suggest, however, that in the infant group, the decrease in superoxide production per unit of neutrophil could be compensated by an increased number of neutrophils in the peripheral blood. Mikawa et al beneficially teach that surgical stress, along with other factors, some of which include hormonal response, prostaglandins, and postoperative pain, can modulate immune system activity with respect to neutrophil response (see, for example, pg. 1164, col. 2; pg. 1165, col. 2; pg. 1167, and 1169).

Mikawa et al does not expressly teach a method wherein superoxide production is detected using luminol as an amplifier and the resulting chemiluminescence in measured.

Pfefferkorn beneficially teaches a method wherein luminol is used to measure the chemiluminescence in superoxide anion assays triggered by PMA or FMLP in cells such as polymorphonuclear nucleocytes (i.e., neutrophils). In particular, Pfefferkorn

beneficially teaches that inducers, in conjunction with luminol chemiluminescence assays for superoxide, are useful for enhancing detection of superoxide (see, Abstract, and col. 4, lines 15-35, and col. 3, lines 50-65).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Mikawa et al based upon the beneficial teachings provided by Pfefferkorn with respect to the art-recognized method of enhancing detection of superoxide anion using an amplifier, such as luminol, when using an inducer, such as FLMP or PMA, as discussed above. Furthermore, Mikawa et al particularly point out that neutrophil production of superoxide is depressed in infants and neonates undergoing surgery compared to basal levels in control samples taken prior to surgery, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Mikawa et al in conjunction with the methods of Pfefferkorn so as to determine whether an individual is experiencing a changed physiological status arising from exposure to a psychological stressor, such as a medical treatment (i.e., surgery) for the expected benefit of being able to positively identify such individuals and to provide a treatment to aid in recovery and fight off possible infection after surgery resulting from reduced neutrophil microbicidal activity. The result-effective adjustment of particular conventional working conditions (e.g., performing the test on a particular type of individual, e.g., mammals other than humans, or on birds) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Response to Amendment and Arguments

The declaration under 37 CFR 1.132 filed 10 December 2007 is insufficient to overcome the 35 U.S.C. 103(a) rejections of claims 1-5, 9-11, and 23-24 based upon Mikawa et al (Can J Anaesth 1993) in view of Pfefferkorn (US 5,492,816) and claims 1-2, 12-14, and 16-17 based upon Mikawa et al (Can J Anaesth 1993) in view of Carlson et al (US 6,319,953) as set forth in the last Office action because: Applicant's main argument with respect to the Mikawa reference is that Mikawa uses isolated neutrophils instead of whole blood, as required by the invention. Applicant asserts in the instant declaration that leukocytes are deliberately kept in the local environment (i.e., suspended in the blood) to allow them to interact with surrounding red cells and between different leukocyte cohorts. The Examiner respectfully disagrees with Applicant's arguments because the instant specification specifically states that "while a whole blood sample may be utilized directly...it will be appreciated that a blood fraction comprising neutrophils may alternatively be employed if desired....For example, a sample comprising isolated leukocytes may be employed" (see page 7, lines 22-26 of instant specification).

Furthermore, Applicant argues that the Mikawa reference does not deal with the same technical problem as the instant invention, because Applicant argues that Mikawa deals with the effect of surgery on neutrophils instead of quantifying psychological stress. The Examiner respectfully disagrees with Applicant's arguments with respect to Mikawa. First, based upon Applicant's lack of a specific definition in the instant specification for "psychological stressor," the broadest reasonable interpretation has been given to the phrase, and therefore, the period of time surrounding a surgical procedure, i.e., the perioperative period, could be considered a psychological stressor. Furthermore, since Applicant does not provide any particular guidance as to what encompasses a "changed physiological status," the teachings of Mikawa would fall under this broad terminology as well.

Applicant further argues that Pfefferkorn only provides enhanced luminol chemiluminescence assays for superoxide. In addition, Applicant argues that the combination of Mikawa and Pfefferkorn do not come close to the claimed invention of a "rapid, objective and physiologically relevant method of quantifying the effect of psychological stressors relying on neutrophils as biomarkers in whole blood samples."

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a method of quantifying the effect of psychological stressors relying on neutrophils as biomarkers) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Based upon the teachings of Mikawa and Pfefferkorn, it would have been both obvious and beneficial to provide a method of measuring superoxide production in neutrophils after exposure to a psychological stressor.

Claims 1-2, 12-14, and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikawa et al (Can J Anaesth 1993) in view of Carlson et al (US 6,319,953).

A method is claimed for determining whether an individual is experiencing changed physiological status arising from exposure to a psychological stressor, further comprising a method for screening a stress-relieving drug, and treating an individual suffering from stress.

Mikawa et al beneficially teach a method wherein a basal level of superoxide production, or control level, is measured in whole blood samples before anesthesia administration prior to a surgical procedure in infants and neonates. Mikawa et al beneficially teach methods wherein PMA and FMLP are used as inducers for production of superoxide in neutrophils. Mikawa et al further beneficially teach that after surgery, neonates had the greatest suppression of superoxide production by neutrophils, but infants also showed immunosuppression after surgery. Mikawa et al did suggest, however, that in the infant group, the decrease in superoxide production per unit of neutrophil could be compensated by an increased number of neutrophils in the peripheral blood. Mikawa et al beneficially teach that surgical stress, along with other factors, some of which include hormonal response, prostaglandins, and postoperative

pain, can modulate immune system activity with respect to neutrophil response (see, for example, pg. 1164, col. 2; pg. 1165, col. 2; pg. 1167, and 1169).

Mikawa et al do not expressly teach a method for screening stress-relieving drugs or treating individuals suffering from stress identified by the methods as taught by Mikawa et al.

Carlson et al beneficially teach a method of screening for a stress-relieving drug, wherein a test compound is administered to an individual and the individual is then exposed to a psychological stressor. Furthermore, Carlson et al beneficially teach that measurements are made to determine the effect of the stress on the individual, and then compared to the individual's own baseline or to other individuals of the same species which receive no test compound. Furthermore, Carlson et al particularly teach a method for treatment of stress (i.e., anxiety) which comprises administration to a patient in need (i.e., a patient suffering from stress) an amount of a compound that gives effective relief of said stress, as determined by the methods taught by Carlson et al (see, for example, Abstract, col. 36, lines 10-65, and col. 42, lines 15-67).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Mikawa et al based upon the beneficial teachings provided by Carlson et al with respect to the art-recognized method of screening for stress-relieving drugs and treating individuals suffering from stress by providing a stress-relieving treatment, as discussed above. Furthermore, Mikawa et al particularly point out that neutrophil production of superoxide is depressed in infants and neonates undergoing surgery compared to basal levels in

control samples taken prior to surgery, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Mikawa et al in conjunction with the methods of Carlson et al so as to determine whether an individual is experiencing a changed physiological status arising from exposure to a psychological stressor, such as a medical treatment (i.e., surgery) for the expected benefit of being able to provide a treatment to aid in recovery and fight off possible infection after surgery resulting from reduced neutrophil microbicidal activity. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made, provided with the teachings of Mikawa et al and Carlson et al, to synthesize a stress-relieving drug identified by the methods of Mikawa et al and Carlson et al, and to administer such a drug to individuals identified by the method of Mikawa et al and to further test the efficacy of such a drug using the methods provided by Carlson et al and Mikawa et al, so as to be able to properly identify individuals exposed to a stressor and treat them with a drug that will alleviate the stress-induced decrease in neutrophil response, which predisposes individuals to infections and other immunosuppressive effects.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Response to Amendment and Arguments

The declaration under 37 CFR 1.132 filed 10 December 2007 is insufficient to overcome the 35 U.S.C. 103(a) rejections of claims 1-5, 9-11, and 23-24 based upon Mikawa et al (Can J Anaesth 1993) in view of Pfefferkorn (US 5,492,816) and claims 1-2, 12-14, and 16-17 based upon Mikawa et al (Can J Anaesth 1993) in view of Carlson et al (US 6,319,953) as set forth in the last Office action because: Applicant's main argument with respect to the Mikawa reference is that Mikawa uses isolated neutrophils instead of whole blood, as required by the invention. Applicant asserts in the instant declaration that leukocytes are deliberately kept in the local environment (i.e., suspended in the blood) to allow them to interact with surrounding red cells and between different leukocyte cohorts. The Examiner respectfully disagrees with Applicant's arguments because the instant specification specifically states that "while a whole blood sample may be utilized directly...it will be appreciated that a blood fraction comprising neutrophils may alternatively be employed if desired....For example, a sample comprising isolated leukocytes may be employed" (see page 7, lines 22-26 of instant specification).

Furthermore, Applicant argues that the Mikawa reference does not deal with the same technical problem as the instant invention, because Applicant argues that Mikawa deals with the effect of surgery on neutrophils instead of quantifying psychological stress. The Examiner respectfully disagrees with Applicant's arguments with respect to

Mikawa. First, based upon Applicant's lack of a specific definition in the instant specification for "psychological stressor," the broadest reasonable interpretation has been given to the phrase, and therefore, the period of time surrounding a surgical procedure, i.e., the perioperative period, could be considered a psychological stressor. Furthermore, since Applicant does not provide any particular guidance as to what encompasses a "changed physiological status," the teachings of Mikawa would fall under this broad terminology as well.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a method of quantifying the effect of psychological stressors relying on neutrophils as biomarkers) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues with respect to Carlson et al that the reference deals with an entirely different technical field and that the combination with Mikawa is not proper and does not suggest the claimed invention. The Examiner respectfully disagrees with Applicant's arguments with respect to the combination of Carlson et al and Mikawa. With respect to Applicant's reference to the example of socially isolated animals in Carlson for whole animal screening, the Examiner would kindly like to point out that Applicant's specification teaches social isolation as a psychological stressor in non-human mammals. It would have been obvious to one of ordinary skill in the art to

combine the teachings of Carlson et al with that of Mikawa to determine whether a drug relieves the stress induced by the psychological stressor, as measured in neutrophils.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMANDA P. WOOD whose telephone number is (571)272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW
Examiner
Art Unit 1657

/Robert B Mondesi/
Primary Examiner, Art Unit 1652
March 27, 2008